Best Available Copy

le: TYPE 2 DIABETES SUSCEPTIBILITY GENES
Inventor(s): Attie/Stoehr/Schueler/Clee
Application No.:
Docket Number: 960296.99080


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Sequence 1: mSorLA       2033 aa     SEQ ID NO: 5
Sequence 2: mSort         825 aa     SEQ ID NO: 6
Sequence 3: Vps10p       1577 aa     SEQ ID NO: 7
Sequence 4: mCS2         1159 aa     SEQ ID NO: 8
Sequence 5: hCS3         1223 aa     SEQ ID NO: 9
Sequence 6: mCS3         1219 aa     SEQ ID NO: 10
Sequence 7: mCS1a        1147 aa     SEQ ID NO: 11
Sequence 8: mCS1b        1167 aa     SEQ ID NO: 12
Sequence 9: mCS1c        1178 aa     SEQ ID NO: 13
Sequence 10: hCS1        1168 aa     SEQ ID NO: 14
Aligning...

Sequences (1:2) Aligned. Score: 20
Sequences (1:3) Aligned. Score: 8
Sequences (1:4) Aligned. Score: 18
Sequences (1:5) Aligned. Score: 16
Sequences (1:6) Aligned. Score: 15
Sequences (1:7) Aligned. Score: 13
Sequences (1:8) Aligned. Score: 14
Sequences (1:9) Aligned. Score: 13
Sequences (1:10) Aligned. Score: 14
Sequences (2:3) Aligned. Score: 16
Sequences (2:4) Aligned. Score: 20
Sequences (2:5) Aligned. Score: 20
Sequences (2:6) Aligned. Score: 20
Sequences (2:7) Aligned. Score: 21
Sequences (2:8) Aligned. Score: 21
Sequences (2:9) Aligned. Score: 20
Sequences (2:10) Aligned. Score: 21
Sequences (3:4) Aligned. Score: 11
Sequences (3:5) Aligned. Score: 11
Sequences (3:6) Aligned. Score: 11
Sequences (3:7) Aligned. Score: 10
Sequences (3:8) Aligned. Score: 11
Sequences (3:9) Aligned. Score: 10
Sequences (3:10) Aligned. Score: 10
Sequences (4:5) Aligned. Score: 42
Sequences (4:6) Aligned. Score: 42
Sequences (4:7) Aligned. Score: 42
Sequences (4:8) Aligned. Score: 42
Sequences (4:9) Aligned. Score: 43
Sequences (4:10) Aligned. Score: 42
Sequences (5:6) Aligned. Score: 92
Sequences (5:7) Aligned. Score: 63
Sequences (5:8) Aligned. Score: 62
Sequences (5:9) Aligned. Score: 64
Sequences (5:10) Aligned. Score: 63
Sequences (6:7) Aligned. Score: 63
Sequences (6:8) Aligned. Score: 62
Sequences (6:9) Aligned. Score: 63
Sequences (6:10) Aligned. Score: 61
Sequences (7:8) Aligned. Score: 98
Sequences (7:9) Aligned. Score: 97
Sequences (7:10) Aligned. Score: 91
Sequences (8:9) Aligned. Score: 96
Sequences (8:10) Aligned. Score: 93
Sequences (9:10) Aligned. Score: 90

CLUSTAL W (1.82) multiple sequence alignment

mSorLA      YA QYLWITFDFCST IHGFSIPFRAAD LLLHSKASNLLL GFDRSHPNKQLW KSDDFGQTWI 60
mSort       ------------------------------------------------------------
Vps10p      ------------------------------------------------------------

mSorLA      MI QEHVKSFSWGID PYDQPNAIYIER HEPFGFSTVLRSTDFFQSRENQEVILEEVRDFQL 120
mSort       ------------------------------------------------------------
Vps10p      FV YSLWALLLIPLI NAEEFTPKVTKT IAQDSFEILSFDDSNTLIRKQDAS VTISFDDGET 65

mSorLA      RD KYMFATKVVHLP GSQQQSSVQLWV SFGRKPMRAAQFVTKHPINEYYIA DAAEDQVFVC 180
mSort       ------------------------------------------MERPRG  AADG------ 10
Vps10p      WE KVEGIEDEITWI YIDPFNRHDRAVATSMYESRLYITNDQGKSWERITLPDSEK---NI 122
mCS2        ----------------------------------MA  HRGPPSAPKRPG PTAPDRSFQA 24
hCS3        -N MEAARTERPAGR PGAPLVRTGLLLLSTWVLAGAEIT WDATGGPGRPAAPASRPPALSP 59
mCS3        -- MEAAGTERPAGWPGAPLARTGLLLLSTWVLAGAEIT WGATGGPGRLVS PASRPPVLPP 58
mCS1a       MG KVGAGDGYSAG- LSALLAGAGLLML-----LAPGVCSSLSCCPPQHPSSTPR----RT 50
mCS1b       MG KVGAGDGSSAG- LSALLAGAGLLML-----LAPGVCSSLSCCPPQHPSSTPR----RT 50
mCS1c       MG KVGAGDGSSAG- LSALLAGAGLLML-----LAPGVCSSLSCCPPQHPSSTPR----RT 50
hCS1        MG KVGAGGGSQAR- LSALLAGAGLLIL-----CAPGVCGGGSCCPSPHPSSAPR----SA 50
                                                                  T50->I

mSorLA      VSHSNNSTNLYISE AEGLKFSLSLEN VLYYSPGGAGSD TLVRYFANEPFA DFHRVEGLQG 240
mSort       ------LLRWPLGLLLLLQLLPPAAV G---QDRLDAPPPPAPPLLRWAGP ---------- 51
Vps10p      SS RGCYIETHPLNK NYFLAKCNYCEK TEVDNEENSGDEEGAPVIFNITRCTDKVFASNDG 182
mCS2        LLPPCWPRSWPLLLLLLVLVAACGAM GRSPQPGRQGPG VQITRLLPAGRT ---------- 74
hCS3        LS PRAVASQWPEELASARRAAVLGRR AGPELLPQQGGG RGGEMQVEAGGTSPAGERRGRG 119
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FIG 2A

tle: TYPE 2 DIABETES SUSCEPTIBILITY GENES
Inventor(s): Attie/Stoehr/Schueler/Clee
Application No.:
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mCS3      LLPRAAENRWPEELASARRAAAPRRRSRLEPL SQASR---GEIR TEAAGMSPEGAR WVPG 115
mCS1a          LT PRGFPHPGPLGR APATPPPLFMR-----PLFAVAPG DRALFLERAGGS ---------R 96
mCS1b          LT PRGFPHPGPLGR APATPPPLFMR-----PLFAVAPG DRALFLERAGGS ---------R 96
mCS1c          LT PRGFPHPGPLGR APATPPPLFMR-----PLFAVAPG DRALFLERAGGS ---------R 96
hCS1           ST PRGFSHQGRPGR APATPLPLVVR-----PLFSVAPG DRALSLERARGT ---------G 96

mSorLA         VY IATLINGSMNEE NMRSVITFDKGGTWEFLQAPAFTGYGEKINCELSQGCSLHLAQRLS 300
mSort          ------VGVSWGLR AAAPGGPVPRAG RWRRGAPAEDQD CGRLP----------------- 88
Vps10p         GK SFSEIKSSLE-R NENSAISISDCG FAKTGKDSDLESSDTSIICLFQNM QLIMDEFSS- 240
mCS2           ---ESGDRKDPQAR ESEPSVPGLGPGSASGPSTDGAPAPGKGRRARAVPVAGAASASR-- 129
hCS3           IPAPAKLGGARRSRRAQPPITQERGD AWATAPADGSR--GSRPLAKGSREEVKAPRAGG- 176
mCS3           IP SPSQAGSARRTRRAQPPSPLERGD SWATALADGAK--GSRPHTKGSREEVRATRTGG- 172
mCS1a          VS VATAARSGRRRR SGTEPEKIEPGE GASRSRRDMLKD GGQQGLGTGARD PGKATRFR-- 154
mCS1b          VS VATAARSGRRRR SGTEPEKIEPGE GASRSRRDMLKD GGQQGLGTGARD PGKATRFR-- 154
mCS1c          VS VATAARSGRRRR SGTEPEKIEPGE GASRSRRDMLKD GGQQGLGTGARD PGKATRFR-- 154
hCS1           AS MAVAARSGRRRR SGADQEKAERGE GASRSPRGVLRD GGQQEPGTRERD PDKATRFR-- 154
                         ^furin?  .          ^furin?   .                    :

mSorLA         QLLNLQLRRMPILS KESAPGLIIATGSVGKNLASKTNV YISSSAGARWRE ALPGPHYYTW 360
mSort          ----------------------------------DFIA KLTNNTHQHVFDDLSGSVSLSW 114
Vps10p         ----------------------------------PYTES KLVLTTDWGKSL KEFDQFKDKV 267
mCS2           ----------------------------------AQV SLISTSFVLKGD ATHNQAMVHW 154
hCS3           --------------------------------SAAEDL RLPSTSFALTGD SAHNQAMVHW 204
mCS3           --------------------------------ASTEEL RLPSTSFALTGD SAHNQAMVHW 200
mCS1a          ---------------------------------MEEL RLTSTTFALTGD SAHNQAMVHW 180
mCS1b          ---------------------------------MEEL RLTSTTFALTGD SAHNQAMVHW 180
mCS1c          ---------------------------------MEEL RLTSTTFALTGD SAHNQAMVHW 180
hCS1           ---------------------------------MEEL RLTSTTFALTGD SAHNQAMVHW 180
               .  . .    .  : ..:::..   ::. : ... :.     :  .:         .

mSorLA         GD HGGIIMAIAQGM ETNELKYSTNEG ETWKTFVFSEKPVFVYGLLTEPGE KSTVFTIFGS 420
mSort          VG DSTGVILVLTTF QVPLVIVSFGQS KLYRSEDYGKN----FKDITNLINNTFIRTEFGM 170
Vps10p         VNGYRILKSHMVVI TQGDRYNDMSSM DVWVSNDLSNFK MAYMPTQLRHSM QGEIYEDAMG 327
mCS2           TG ENSSVILILTKYYH-ADMGKVLESSLWRSSDFGTT----YTKLTLQPG VTTVIDNF-- 207
hCS3           SGHNSSVILILTKL YD-FNLGSVTESSLWRSTDYGTT----YEKLNDKVG LKTVLSYL-- 257
mCS3           SGHNSSVILILTKL YD-FNLGSVTESSLWRSVDYGAT----YEKLNDKVG LKTVLSYL-- 253
mCS1a          SGHNSSVILILTKL YD-YNLGSITESSLWRSTDYGTT----YEKLNDKVG LKTILSYL-- 233
mCS1b          SGHNSSVILILTKL YD-YNLGSITESSLWRSTDYGTT----YEKLNDKVG LKTILSYL-- 233
mCS1c          SGHNSSVILILTKL YD-YNLGSITESSLWRSTDYGTT----YEKLNDKVG LKTILSYL-- 233
hCS1           SGHNSSVILILTKL YD-YNLGSITESSLWRSTDYGTT----YEKLNDKVG LKTILGYL-- 233
                .     :                .  .  . : :   .                    :

mSorLA         NK ESVHSWLILQVN ATDALGVPCTEN DYKLWSPSDERGNECLLGHKTVFKRRTPHATCFN 480
mSort          --------------------AIGPENSGKVILTAEVSG ---------------------- 188
Vps10p         -------------------RIILPMS RERSDQEED------------------------- 343
mCS2           --------------------YICPAN KRKIILVSSSL---------------------- 224
hCS3           -------------------YVNPTN KRKIMLLSD------------------------- 272
mCS3           -------------------YVNPTN KRKIMLLSD------------------------- 268
mCS1a          -------------------YVCPTN KCKIMLLTD------------------------- 248
mCS1b          -------------------YVCPTN KCKIMLLTD------------------------- 248
mCS1c          -------------------YVCPTN KCKIMLLTD------------------------- 248
hCS1           -------------------YVCPTN KRKIMLLTD------------------------- 248
               ...:  :    . . ::.:     . .  :     .  ....  . .:  .  :. ::. .

mSorLA         GEDFDRPVVVSNCSCTREDYECDFGF KMSEDLSLEVCVPDPEFFGKPYSPPVPCPVGSSY 540
mSort          GS RGGRVFRSSDFA KNFVQTDLPFHP -----LTQMMYS PQNSDYLLALST ENGLWVSKNF 243
Vps10p         KG IVSEILISDSQG LKFSPIPWTANE VFG-YINLYQPTYLKGTMIASLYPLSRRRNRKGK 402
mCS2           GD REQSLFLSTDEG ATFQKYPVPFL------VETLLFH PKEEDKVLAYTK DSKLYVSSDL 278
```

FIG 2B

```
hCS3        PEMESSILISSDEGATYQKY RLTFY------I QSLLFHPKQEDWVLAYSLDQKLYSSMDF 326
mCS3             PE MESSVLISSDEG ATYQKYRLTFY------IQSLLFH PKQEDWVLAYSL DQKLYSSMDF 322
mCS1a            PE IESSLLISSDEG ATYQKYRLNFY------LQSLLFH PKQEDWILAYSQ DQKLYSSAEF 302
mCS1b            PE IESSLLISSDEG ATYQKYRLNFY------LQSLLFH PKQEDWILAYSQ DQKLYSSAEF 302
mCS1c            PE IESSLLISSDEG ATYQKYRLNFY------LQSLLFH PKQEDWILAYSQ DQKLYSSAEF 302
hCS1             PE IESSLLISSDEG ATYQKYRLNFY------IQSLLFH PKQEDWILAYSQ DQKLYSSAEF 302
                            .  . . .              .. :              .

mSorLA           RR TRGYRKISGDTCSGGDVEARLEGE LVPCPLAEENEFILYAMRKFIYRY DLASGATEQL 600
mSort            G--EKWEEIHK---------AVCLAK WGPNNIIFFTTH VNGSCKADLGAL ELWRTSDLGK 292
Vps10p           AK GVKNKGVTKISV DNGLTWTVLKVV DPDNADSFDCDI TDFENCSLQNMF YTREGSTPTA 462
mCS2             G--KKWTLLQERVT KDHVFWAVSGVDDDPNLVHVEAQD LSGGYRYYTCLI YNCSAQPHIA 336
hCS3             G--RRWQLMHERIT PNRFYWSVAGLD KEADLVHMEVRTTDGYAHYLTCRI QECAETTRSG 384
mCS3             G--RRWQLMHERIT PNRFYWSVSGLD KEADLVHMEVRT ADGYAHYLTCRI QECAETTRSG 380
mCS1a            G--RRWQLIQESVVPNRFYWSVMGSS KEPDLVHLEART VDGHSIYLTCRM QNCTEANRNK 360
mCS1b            G--RRWQLIQESVVPNRFYWSVMGSS KEPDLVHLEART VDGHSIYLTCRM QNCTEANRNK 360
mCS1c            G--RRWQLIQESVVPNRFYWSVMGSS KEPDLVHLEART VDGHSIYLTCRM QNCTEANRNK 360
hCS1             G--RRWQLIQEGVVPNRFYWSVMGSN KEPDLVHLEART VDGHSHYLTCRM QNCTEANRNQ 360
                           :      .    :

mSorLA           PL SGLRAAVALDFGYERNCLYWSDLALDTIQRLCLNGSTGQEVIINSGLE TVEALAFEPL 660
mSort            TF KTIG-------------------------------------VKIYSFG LGGRFLFASE 315
Vps10p           GILMTTG-----IV GDGSVFDWGDQR TFISRDGGLTWK LAFDFPCLYAVG DYGNVIVAIP 517
mCS2             PF SGP--------------------------------------IDRGSLT VQDEYIFLKA 358
hCS3             PFARS---------------------------------------IDISSLVVQDEYIFIQV 406
mCS3             PFARS---------------------------------------IDISSLVVQDEYIFIQV 402
mCS1a            PFPGY---------------------------------------IDPDSLIVQDDYVFVQL 382
mCS1b            PFPGY---------------------------------------IDPDSLIVQDDYVFVQL 382
mCS1c            PFPGY---------------------------------------IDPDSLIVQDDYVFVQL 382
hCS1             PFPGY---------------------------------------IDPDSLIVQDHYVFVQL 382
                  :    .: : .   . .    ..           . .  . .     ..       .

mSorLA           SQ LLYWVDAGFKKI EVANPDGDFRLT IVNSSVLDRPRALVLVPQEGVMFW TDWGDLKPGI 720
mSort            MA DK---DTTRRIH VSTDQGDTWSMA QLPSVGQEQFYS ILAANEDMVFMH VDE------- 365
Vps10p           YN ADEDDDPQSEFYYSLDQGKTWTEYQLETTIYPNEVM NTTPDGSGAKFILNG------F 571
mCS2             TS ------TNRTKYYVSYRRSDFVLM KLPKYALPKDLQ IISTDEQQVFVAVQE------- 405
hCS3             TT ------SGRASYYVSYRREAFAQI KLPKYSLPKDMH IISTDENQVFAAVQE------- 453
mCS3             TI ------GGRASYYVSYRREAFAQI KLPKYSLPKDMH IISTDENQVFAAVQE------- 449
mCS1a            TS ------GGRPHYYVSYRRSPFAQM KLPKYALPKDMH VISTDENQVFAAVQE------- 429
mCS1b            TS ------GGRPHYYVSYRRSPFAQM KLPKYALPKDMH VISTDENQVFAAVQE------- 429
mCS1c            TS ------GGRPHYYVSYRRSPFAQM KLPKYALPKDMH VISTDENQVFAAVQE------- 429
hCS1             TS ------GGRPHYYVSYRRNAFAQM KLPKYALPKDMH VISTDENQVFAAVQE------- 429
                        .              :    : .    .          . .    : .. ...

mSorLA           YR SYMDGSAAYRLV SEDVKWPNGISV DS---------- QWIYWTDAYLDC IERITFSGQQ 770
mSort            ---PGDTGFGTIFT SDDRGIVYSKSL DR---------- HLYTTTGG---E TDFTNVTSLR 409
Vps10p           TLAHMDGTTNFIYAIDFSTAFNDKTC EENDFEDWNLAE GKCVNGVKYKIRRRKQDAQCLV 631
mCS2             ---WNQVDTYNLYQSDLRGVRYSLVL EN---------- VRSSRQAEENVVIDILEVRGVK 452
hCS3             ---WNQNDTYNLYI SDTRGIYFTLAM EN---------- IKSSRGLMGNIIIELYEVAGIK 500
mCS3             ---WNQNDTYNLYI SDTRGIYFTLAM EN---------- IKSSRGLMGNIIIELYEVAGIK 496
mCS1a            ---WNQNDTYNLYI SDTRGVYFTLAL EN---------- VRSSRGPEGNVMIDLYEVAGIK 476
mCS1b            ---WNQNDTYNLYI SDTRGVYFTLAL EN---------- VRSSRGPEGNVMIDLYEVAGIK 476
mCS1c            ---WNQNDTYNLYI SDTRGVYFTLAL EN---------- VRSSRGPEGNVMIDLYEVAGIK 476
hCS1             ---WNQNDTYNLYI SDTRGVYFTLAL EN---------- VQSSRGPEGNIMIDLYEVAGIK 476
```

FIG 2C

tle: TYPE 2 DIABETES SUSCEPTIBILITY GENES
Inventor(s): Attie/Stoehr/Schueler/Clee
Application No.:
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```
mSorLA    RSVILDSLPHPYAIAVFKNEIYWDDWSQLSIFRASKHSRSQVEILASQLTGLMDMKVFYK 830
mSort          GVYITSTLSEDNSIQSMITFDQGGRWEHLRKP-ENSKCDA---------------------- 448
Vps10p         KKVFEDLQLFETACDKCTEADYECAFEFVRDATGKCVPDYN-----------------L 673
mCS2           GVFLAN-QKVDGKVTTVITYNKGRDWDYLRPPSTDMNGKP---------------------- 491
hCS3           GIFLAN-KKVDDQVKTYITYNKGRDWRLLQAPDVDLRGSP---------------------- 539
mCS3           GIFLAN-KKVDDQVKTYITYNKGRDWRLLQAPDVDLRGSP---------------------- 535
mCS1a          GMFLAN-KKIDNQVKTFITYNKGRDWRLLQAPDADLRGDP---------------------- 515
mCS1b          GMFLAN-KKIDNQVKTFITYNKGRDWRLLQAPDADLRGDP---------------------- 515
mCS1c          GMFLAN-KKIDNQVKTFITYNKGRDWRLLQAPDADLRGDP---------------------- 515
hCS1           GMFLAN-KKIDNQVKTFITYNKGRDWRLLQAPDTDLRGDP---------------------- 515

mSorLA         GKNAGSNACVPQPCSLLCLPKANNSKSCRCPEGVASSVLPSGDLMCDCPQGYQRKNNTCV 890
mSort          ------TAKNKNECSLHIHASYSISQKLNVPMAPLSEPNAVGIVIAHG------------ 490
Vps10p         IVLSDVCDKTKKKTVPVKPLQLVKGDKCKKPMTVKSVDISCEGVPKKG------------ 721
mCS2           ------TNCQPPDCYLHLHLRWADNPYVSGTVH--TKDTAPGLIMGAG------------ 531
hCS3           ------VHCLLPFCSLHLHLQLSENPYSSGRIS--SKETAPGLVVATG------------ 579
mCS3           ------VHCLLPFCSLHLHLQLSENPYSSGRIS--SKDTAPGLVVATG------------ 575
mCS1a          ------VHCLLPYCSLHLHLKVSENPYTSGIIA--SRDTAPSIIVASG------------ 555
mCS1b          ------VHCLLPYCSLHLHLKVSENPYTSGIIA--SRDTAPSIIVASG------------ 555
mCS1c          ------VHCLLPYCSLHLHLKVSENPYTSGIIA--SRDTAPSIIVASG------------ 555
hCS1           ------VHCLLPYCSLHLHLKVSENPYTSGIIA--SKDTAPSIIVASG------------ 555

mSorLA         KEENTCLRNQYRCSNGNCINSIWWCDFDNDCGDMSDERNCPTTVCDADTQFRCQESGTCI 950
mSort          ------------------------------------------------------------
Vps10p         ------------------------------------------------------------
mCS2           ------------------------------------------------------------
hCS3           ------------------------------------------------------------
mCS3           ------------------------------------------------------------
mCS1a          ------------------------------------------------------------
mCS1b          ------------------------------------------------------------
mCS1c          ------------------------------------------------------------
hCS1           ------------------------------------------------------------

mSorLA         PLSYKCDLEDDCGDNSDESHCEMHQCRSDEFNCSSGMCIRSSWVCDGDNDCRDWSDEANC 1010
mSort          ----------SVGDAISVMVPDVYISD-----------------DGGYSWAKMLEGPHY 522
Vps10p         ----------TNDKEIVVTENKFDFKIQFYQYFDTVTDESLLMINSRGEAYISHDGGQTI 771
mCS2           ----------NLGSQLVEYKEEMYITS-----------------DCGHT WRQVFEEEHH 563
hCS3           ----------NIGPELSYTDIGVFISS-----------------DGGNTWRQIFDEEYN 611
mCS3           ----------NIGSELSYTDIGVFISS-----------------DGGNTWRQIFDEEYN 607
mCS1a          ----------NIGSELSDSDISMFVSS-----------------DAGNTWRQIFEEEHS 587
mCS1b          ----------NIGSELSDSDISMFVSS-----------------DAGNTWRQIFEEEHS 587
mCS1c          ----------NIGSELSDSDISMFVSS-----------------DAGNTWRQIFEEEHS 587
hCS1           ----------NIGSELSDTDISMFVSS-----------------DAGNTWRQIFEEEHS 587

mSorLA         TAIYHTCEASNFQCHNGHCIPQRWACDGDADCQDGSDEDPVSCEKKCNGFHCPNGTCIPS 1070
mSort          YTILDSGGIIVAIEHSNRPINVIKFSTDEGQC-----------------WQSYVFTQE 563
Vps10p         RRFDSNGETIIEVVFNPYYNSSAYLFGSKGSIFS--------------THDRGYSFMTA 816
mCS2           VLYLDHGGVIAAIKDTSIPLKILKFSVDEGHT-----------------WSTHNFTST 604
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FIG 2D

itle: TYPE 2 DIABETES SUSCEPTIBILITY GENES
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Application No.:
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```
hCS3      VWFLDWGGALVAMKHTPLPVRH LWVSFDEGHS------------------WDKYGFTSV 652
mCS3            VWFLDWGGALVAMK HTPLPVRHLWVS FDEGHS------------------WDKYGFTLL 648
mCS1a           IL YLDQGGVLVAMK HTSLPIRHLWLS FDEGRS------------------WSKYSFTSI 628
mCS1b           IL YLDQGGVLVAMK HTSLPIRHLWLS FDEGRS------------------WSKYSFTSI 628
mCS1c           IL YLDQGGVLVAMK HTSLPIRHLWLS FDEGRS------------------WSKYSFTSI 628
hCS1            VL YLDQGGVLVAMK HTSLPIRHLWLS FDEGRS------------------WSKYSFTSI 628
                                .           ...   ..:.... :.......

mSorLA          SK HCDGLRDCPDGS DEQHCEPFCTRFMDFVCKNRQQCLFHSMVCDGIVQC RDGSDEDAAF 1130
mSort           PI YFTGLASEPGA---------------------------------------------- 576
Vps10p          KLPEARQLGMPLDF N---------------------------------------------- 831
mCS2            SVFVDGLLSEPGD---------------------------------------------- 617
hCS3            PLFVDGALVEAGM---------------------------------------------- 665
mCS3            PLFVDGALVEAGV---------------------------------------------- 661
mCS1a           PLFVDGVLGEPGE---------------------------------------------- 641
mCS1b           PLFVDGVLGEPGE---------------------------------------------- 641
mCS1c           PLFVDGVLGEPGE---------------------------------------------- 641
hCS1            PLFVDGVLGEPGE---------------------------------------------- 641
                          .    ... ... .:   .  ... ...   :  ...  ..  ..:...::

mSorLA          AGCSQDPEFHKECDEFGFQCQNGVCI SLIWKCDGMDDCGDYSDEANCENP TEAPNCSRYF 1190
mSort           ------------------------------RSMNISIW GFTESFITRQWV SYTVDFKDIL 606
Vps10p          ---------------AKAQDTFIYYGGKNCESILSPECHAVAYLTNDGGE TFTEMLDNAI 876
mCS2            ------------------------------ETLVMTVF GHIS--FRSDWE LVKVDFRPSF 645
hCS3            ------------------------------ETHIMTVF GHFS--LRSEWQ LVKVDYKSIF 693
mCS3            ------------------------------ETHIMTVF GHFS--LRSEWQ LVKVDYKSIF 689
mCS1a           ------------------------------ETLIMTVF GHFS--HRSEWQ LVKVDYKSIF 669
mCS1b           ------------------------------ETLIMTVF GHFS--HRSEWQ LVKVDYKSIF 669
mCS1c           ------------------------------ETLIMTVF GHFS--HRSEWQ LVKVDYKSIF 669
hCS1            ------------------------------ETLIMTVF GHFS--HRSEWQ LVKVDYKSIF 669
                :..:....  .....   .       .   .                              :

mSorLA          QF HCENGHCI PNRW KCDRENDCGDWS DEKDCGDSHVLP SPTPGPSTCLPNYFRCSSGACV 1250
mSort           ER NCE-------------EDDYTTWLAHSTD--------------------PGDYKDGCI 633
Vps10p          HC EFAGSLFKYPSN EDMVMCQVKEKSSQTRSLVSSTDFFQDDKNTVFENI IGYLSTGGYI 936
mCS2            PR QCG-------------EDDYSSWD LTDL-----------------------QGDHCI 668
hCS3            SR HCT-------------KEDYQTWH LLN------------------------QGEPCV 715
mCS3            SRRCT--------------KEDFETWH LLN------------------------QGEPCV 711
mCS1a           DRRCA--------------EEDYRPWQ LHS------------------------QGEACI 691
mCS1b           DRRCA--------------EEDYRPWQ LHS------------------------QGEACI 691
mCS1c           DRRCA--------------EEDYRPWQ LHS------------------------QGEACI 691
hCS1            DRRCA--------------EEDYRPWQ LHS------------------------QGEACI 691
                  .  ..        .     :           :          :              :

mSorLA          MGTWVCDGYRDCAD GSDEEACPSLANSTAASTPTQLGQCDRFEFECHQPKKCIPNWKRCD 1310
mSort           LG ---------------------------------------------------YKEQFLRLR 644
Vps10p          IVAVPHE-----------------------------------------NNELRAYVTID 954
mCS2            MG ---------------------------------------------------QQRSYRKRK 679
hCS3            MG ---------------------------------------------------ERKIFKKRK 726
mCS3            MG ---------------------------------------------------ERKIFKKRK 722
mCS1a           MG ---------------------------------------------------AKRIYKKRK 702
mCS1b           MG ---------------------------------------------------AKRIYKKRK 702
mCS1c           MG ---------------------------------------------------AKRIYKKRK 702
hCS1            MG ---------------------------------------------------AKRIYKKRK 702
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FIG 2E

tle: TYPE 2 DIABETES SUSCEPTIBILITY GENES
Inventor(s): Attie/Stoehr/Schueler/Clee
Application No.:
Docket Number: 960296.99080


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mSorLA     GHQDCQDGQDE ANCPTHSTLTCTSREFKCEDGEAC IVLSERCDGFLD CSDESDEKACSDE 1370
mSort           KSSVCQNGRDYVVA KQPSVCPCSLED FLCDFGYFRPEN AS------ECVE QPELKGHELE 698
Vps10p          GT EFAEAKFPYDED VGKQEAFTILES EKGSIFLHLATN LVPGRDFGNLLK SNSNGTSFVT 1014
mCS2            STSWCVKGRSFTSALTSRVCKCRDSD FLCDYGFERSSSSESTA--NKCSA NFWFNPLSPP 737
hCS3            PG AQCALGRDHSGS VVSEPCVCANWD FECDYGYERHGE SQ-------CVPAFWYNPASPS 779
mCS3            PG AQCALGREYSGS VVSEPCVCADWD FECDYGYERHGE SQ-------CVPAFWYNPASPS 775
mCS1a           SE RKCMQ--KYAGAMESEPCVCTEAD FDCDYGYERHSNGQ-------CLPAFWFNPSSLS 753
mCS1b           SE RKCMQ--KYAGAMESEPCVCTEAD FDCDYGYERHSNGQ-------CLPAFWFNPSSLS 753
mCS1c           SE RKCMQ--KYAGAMESEPCVCTEAD FDCDYGYERHSNGQ-------CLPAFWFNPSSLS 753
hCS1            SE RKCMQG-KYAGAMESEPCVCTEAD FDCDYGYERHSNGQ-------CLPAFWFNPSSLS 754

mSorLA          LT VYKVQNLQWTAD FSGDVTLTWMRP KKMPSASCVYNV YYRVVGESIWKT LETHSNKTST 1430
mSort           FC LYGKEEHLTTNGYR-----------KIPGDKCQGGM N----------PAREVK----- 732
Vps10p          LE HAVNRNTFGYVD FEKIQGLEGIIL TNIVSNSDKVAE NKEDKQLKTKIT FNEGSDWN-- 1072
mCS2            ED CVLGQTYTSSLGYR-----------KVVSNVCEGGV DLQQSPVQLQCPLQAPR----- 781
hCS3            KD CSLGQSYLNSTGYR-----------RIVSNNCTDGL REKYTAKAQMCP GKAPR----- 823
mCS3            KD CSLGQSYLNSTGYR-----------RIVSNNCTDGL RDKYSAKTQLCP GKAPR----- 819
mCS1a           KD CSLGQSYLNSAGYR-----------KVVSNNCTDGV REQYTAKPQKCP GKAPR----- 797
mCS1b           KD CSLGQSYLNSAGYR-----------KVVSNNCTDGV REQYTAKPQKCP GKAPR----- 797
mCS1c           KD CSLGQSYLNSAGYR-----------KVVSNNCTDGV REQYTAKPQKCP GKAPR----- 797
hCS1            KD CSLGQSYLNSTGYR-----------KVVSNNCTDGV REQYTAKPQKCP GKAPR----- 798

mSorLA          VL KVLKPDTTYQVK VQVHCLNKVHNTNDFVTLRTPEGLPDAPRNLQLSLN REEEGVILGH 1490
mSort           --------------------------DLKKKCTSNFL NPTKQN---------------- 749
Vps10p          ----------------FLKPPKRDS EGKKFFCSSKSL DECSLHLHGYTE RKDIRDTYSS 1115
mCS2            --------------------------GLQVSIRGEAVAVRPREDVLFVV RQEQGDVLTT 814
hCS3            --------------------------GLHVVTTDGRLVAEQGHNATFIILMEEGDLQRT 856
mCS3            --------------------------GLHVVTTDGRLVAEQGHNATFIILMEEGDLQRT 852
mCS1a           --------------------------GLRIVTADGKL TAEQGHNVTLMV QLEEGDVQRT 830
mCS1b           --------------------------GLRIVTADGKL TAEQGHNVTLMV QLEEGDVQRT 830
mCS1c           --------------------------GLRIVTADGKL TAEQGHNVTLMV QLEEGDVQRT 830
hCS1            --------------------------GLRIVTADGKL TAEQGHNVTLMV QLEEGDVQRT 831

mSorLA          WAPPVHTHGLIREY IVEYSRSGSKMWASQRAASNSTEI KNLLLNALYTVR VAAVTSRGIG 1550
mSort           ----------------SKSNSVPIILAIVGLMLVTVVAG------------------- 772
Vps10p          GS ALGMMFGVGNVG PNLLPYKECSTFFTTDGGETWAEV KKTPHQWEYGDHGGILVLVPEN 1175
mCS2            KYQVDLGDGFKAMY VNLTLTGEPIRHHYESPGIYRVSV RAENMAGHDEAVLFVQVNSPLQ 874
hCS3            NI QLDFGDGIAVSY ANFSPIEDGIKH VYKSAGIFQVTA YAENNLGSDTAVLFLHVVCPVE 916
mCS3            NI QLDFGDGVAVSY ANFSPIEDGIRH VYKSAGIFQVTA YAENNLGSDTAFLFLHVVCPVE 912
mCS1a           LI QVDFGDGIAVSY VNLSSMEDGIKH VYQNVGIFRVTV QVDNSLGSDSAVLYLHVTCPLE 890
mCS1b           LI QVDFGDGIAVSY VNLSSMEDGIKH VYQNVGIFRVTV QVDNSLGSDSAVLYLHVTCPLE 890
mCS1c           LI QVDFGDGIAVSY VNLSSMEDGIKH VYQNVGIFRVTV QVDNSLGSDSAVLYLHVTCPLE 890
hCS1            LI QVDFGDGIAVSY VNLSSMEDGIKH VYQNVGIFRVTV QVDNSLGSDSAVLYLHVTCPLE 891

mSorLA          NW SDSKSITTIKGK VIQAPNIHIDSY DENSLSFTLTMD GDIKVNGYVVNLFWSFDAHKQE 1610
mSort           ----------------------------------------------VLIVKKYVCGGR- 784
Vps10p          SE TDSISYSTDFGK TWKDYKFCADKVLVKDITTVPRDS ALRFLLFGEAAD IGGSSFRTYT 1235
mCS2            AL YLEVVPVIGVNQ EVNLTAVLLPLN PNLTVFYWWIGHSLQPLLSLDNSV TTKFTDAGDV 934
```

FIG 2F

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hCS3      HVHLRVPFVAIRNKEVNISAVVWPSQLGTLTYFWWFGNSTKPLITL DSSISFTFLAEGTD 976
mCS3           HV HLRVPFVAIRNK DVNISAVVWPSQ LGTLTYFWWFGNSTKPLITLDSSI SFTFLAEGTN 972
mCS1a          HV HLSLPFVTTKNK EVNATAVLWPSQ VGTLTYVWWYGNNTEPLITLEGSI SFKFTSEGMN 950
mCS1b          HV HLSLPFVTTKNK EVNATAVLWPSQ VGTLTYVWWYGNNTEPLITLEGSI SFKFTSEGMN 950
mCS1c          HV HLSLPFVTTKNK EVNATAVLWPSQ VGTLTYVWWYGNNTEPLITLEGSI SFKFTSEGMN 950
hCS1           HV HLSLPFVTTKNK EVNATAVLWPSQ VGTLTYVWWYGNNTEPLITLEGSI SFRFTSEGMN 951
                              ..  .

mSorLA         KK TLSFRGGSALSH KVSNLTAHTSYE ISAWAKTDLGDS PLAFEHILTRGSSPPAPSLKAK 1670
mSort          ----FLVHRYSVLQQHAEADGVEALD STSHAKSGYHDD---------------------- 818
Vps10p         ID FRNIFERQCDFD ITGKESADYKYS PLSSKSNCLFGHQT---------------------- 1275
mCS2           RV TVQAACGNSVLQ DSRLVRVLDQFQ VVPLRFSRELDT---------------------- 972
hCS3           TI TVQVAAGNALIQ DTKEIAVHEYFQSQLLSFSPNLDY---------------------- 1014
mCS3           TI TVQVAAGNALIQ DTKEIAVHEYFQSQLLSFSPNLDY---------------------- 1010
mCS1a          TI TVQVSAGNAILQ DTKTIAVYEEFR SLRLAFSPNLDD---------------------- 988
mCS1b          TI TVQVSAGNAILQ DTKTIAVYEEFR SLRLAFSPNLDD---------------------- 988
mCS1c          TI TVQVSAGNAILQ DTKTIAVYEEFR SLRLAFSPNLDD---------------------- 988
hCS1           TI TVQVSAGNAILQ DTKTIAVYEEFR SLRLSFSPNLDD---------------------- 989
                          .  .                    .   .   : .   : .::..:.: .:.

mSorLA         AI NQTAVECIWTGP KNVVYGIFYATS FLDLYRNPKSVTTSLHNKTVIVSK DEQYLFLVRV 1730
mSort          ----------------------------------------SDEDLLE------------ 825
Vps10p         ----------------------------------------EFLRKTDENC  FIGNIPLSEF 1295
mCS2           ----------------------------------------FNPNTPEWR  EDVGLVVTRL 991
hCS3           ----------------------------------------HNPDIPEWRKDIGNVIKRA 1033
mCS3           ----------------------------------------HNPDIPEWR  QDIGNVIKRA 1029
mCS1a          ----------------------------------------YNPDIPEWRRDISRVIKKS 1007
mCS1b          ----------------------------------------YNPDIPEWRRDISRVIKKS 1007
mCS1c          ----------------------------------------YNPDIPEWRRDISRVIKKS 1007
hCS1           ----------------------------------------YNPDIPEWRRDIGRVIKKS 1008
               : ..:: ..  :.... .  ::: .  ...: :::

mSorLA         LIPYQGPSSDYVVV KMIPDSRLPPRH LHAVHIGKTSALIKWESPYDSPDQ DLFYAIAVKD 1790
mSort          ------------------------------------------------------------
Vps10p         SR NIKNCSCTRQDF ECDYNFYKANDGTCKLVKGLSPAN AADVCKKEPDLI EYFESSGYRK 1355
mCS2           LS KETSIPEELLVT VVKPGLPTIADL YVLLPLPRPTRKRSLTS--DKRLAAVQQALNSHR 1049
hCS3           LV KVTSVPEDQILIAVFPGLPTSAELFILPPKNLTERRKGNEGDLEQIVE TLFNALNQNL 1093
mCS3           LI KVTSVPEDQILVAVFPGLPTSAELFILPPKNLTERRKGHEGDLEQIVE TLFNALNQNL 1089
mCS1a          LV EATGIPSQHILVAVLPGLPTAAELFVLPYQDGTREN KRSPEDLEQISE VLIHKLNQNL 1067
mCS1b          LV EATGIPSQHILVAVLPGLPTAAELFVLPYQDGTREN KRSPEDLEQISE VLIHKLNQNL 1067
mCS1c          LV EATGIPSQHILVAVLPGLPTAAELFVLPYQDGTREN KRSPEDLEQISE VLIHKLNQNL 1067
hCS1           LV EATGVPGQHILVAVLPGLPTTAELFVLPYQDPAGEN KRSTDDLEQISE LLIHTLNQNS 1068
                    . .          .              .          .

mSorLA         LI RKTDRSYKVRSR NSTVEYSLSKLE PGGKYHIIVQLGNMSKDSSIKITT VSLSAPDALK 1850
mSort          ------------------------------------------------------------
Vps10p         IPLSTCEGGLKLDAPSSPHACPGK----------EKE FKEKYSVSAGPFAFIFISILLI 1404
mCS2           IS FILRGGLRILVE LRDTDTGP-----------------QRPGGSGG-Y WAVVVLFVIG 1090
hCS3           VQ FELKPGVQVIVY VTQLTLAP-----------------LVDSSAGHSSSAMLMLLSVV 1135
mCS3           VQ FELKPGVQVIVY VTQLTLAP-----------------LVDSSAGHSSSAMLMLLSVV 1131
mCS1a          VH FELKPGVQVLVH AAHLTAAP-----------------LVDLTPTHSGSAMLMLLSVV 1109
mCS1b          VH FELKPGVQVLVH AAHLTAAP-----------------LVDLTPTHSGSAMLMLLSVV 1109
mCS1c          VH FELKPGVQVLVH AAHLTAAP-----------------LVDLTPTHSGSAMLMLLSVV 1109
hCS1           VH FELKPGVRVLVH AAHLTAAP-----------------LVDLTPTHSGSAMLMLLSVV 1110
```

FIG 2G

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                                .              .. .....      .            .  ^ trans-

mSorLA       II TENDHVLLFWKS LALKEKQFNETR GYEIHMSDSAVN LTAYLGNTTDNFFKVSNLKMGH 1910
mSort        ------------------------------------------------------------
Vps10p       IFFAAWFVYDRGIRRNGGFARFGEIR LGDDGLIENNNT DRVVNNIVKSGF YVFSNIGSLL 1464
mCS2         LFAVGAFILYKFKRKRPGRTVYAQMHNEKEQEMTSPVSHSEDAQSTMQGNHSGVVLSINS 1150
hCS3         FV GLAVFLIYKFKRKIPWINIYAQVQHDKEQEMIGSVSQSENAPKITLSD FT-EPEELLD 1194
mCS3         FV GLAVFLIYKFKRKIPWINIYAQVQHDKEQEMIGSVSQSENAPKITLSD FT-EPEELLD 1190
mCS1a        FV GLAVFVIYKFKR-----CVFLLLP-------------SYPRPPPPSSF CQ-VQKQ--- 1147
mCS1b        FV GLAVFVIYKFKRR----VALPSPP SPSAQPGDSSLR LQRPRPATPPSS PK-RGSAGAQ 1164
mCS1c        FV GLAVFVIYKFKRKIPGINVYAQMQNEKEQELINPVSHSESRPSVPHPD LR-RPGQLVD 1168
hCS1         FV GLAVFVIYKFKRR----VALPSPP SPSTQPGDSSLR LQRARHATPPST PK-RGSAGAQ 1165
              -membrane^                              .S1149->P      .

mSorLA       NYTFTVQARCLFGSQICGEPAVLLYDELSSGADAAVIQ AARSTDVAAVVVPILFLILLSL 1970
mSort        ------------------------------------------------------------
Vps10p       QHTKTNIAHVISKI RGRFGNRTGPSYSSLIHDQFLDEA DDLLAGHDEDAN--DLSSFMDQ 1522
mCS2         RE MHSYLVG---------------------------------------------------- 1159
hCS3         KE LDTRVIGGIATIANSESTKEIPNCTSV-------------------------------- 1223
mCS3         KE LDTRVIGSIATIASSESTKEIPNCTSV-------------------------------- 1219
mCS1a        ------------------------------------------------------------
mCS1b        FAI--------------------------------------------------------- 1167
mCS1c        EK VESQLLGK------------------------------------------------- 1178
hCS1         YAI--------------------------------------------------------- 1168
                 :                       .              :.        .       .

mSorLA       GV GFAILYTKHRRL QSSFSAFANSHYSSRLGSAIFSSG DDLGEDDEDAPMITGFSDDVPM 2030
Vps10p       GSNFEIEEDDVPTL EEEHTSYTDQPTTTDVPDALPEGN EENIDRPDSTAP SNENQ----- 1577
. .     .     ... :: :..  ::   .:  .....   .  ..:.  .   ... .

mSorLA       VIA 2033
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FIG 2H

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